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10/594,160	05/24/2007	Helge H. Rasmussen	U 016502-0	8069

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EXAMINER	
PHILLIPS JR, WELDON P	
ART UNIT	PAPER NUMBER
4121	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,160	RASMUSSEN ET AL.	
	Examiner	Art Unit	
	WELDON PHILLIPS JR.	4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 15-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/31/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application for patent entered the national stage in the United States of America under 35 USC 371 from PCT/AU05/000590, filed April 26, 2005, claiming benefit from Australian Provisional Application No. 2004902179, filed April 23, 2004.

All claims receive the benefit of said Australian filing date.

Claim Status

Applicant's election of Group II, consisting of claims 3-14, in the reply filed on January 16, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1, 2 and 15-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on January 16, 2009. Examiner acknowledges receipt of the listing of claims designating the withdrawn claims on January 16, 2009.

Applicant's election of several species in the reply filed on January 16, 2009 is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Upon further consideration, examiner has determined that no examination and search burden exists for these patentably distinct species. As such, the species election is vacated.

Information Disclosure Statement

One Information Disclosure Statements (IDS) was filed by applicant on May 31, 2007 in compliance with 37 CFR § 1.97, 37 CFR § 1.98 and MPEP § 609. The record has been amended to reflect that all documents contained therein have been considered by the examiner.

Acknowledgement

Receipt of copies of the International Search Report and the International Preliminary Report on Patentability, reflecting the International Searching Authority's non-binding opinion regarding novelty, inventive step and industrial applicability, is acknowledged and the contents of said reports have been considered by the examiner to the extent possible.

A copy of Australian Provisional Application No. 2004902179, filed April 23, 2004, has been received and considered by the examiner.

Specification

The specification has not been proofed to the extent necessary to uncover the presence of all minor errors. At this time, applicant's cooperation is requested in correcting any and all errors of which applicant is or may become aware of in the specification.

Claim Objections

Claim 5 is missing a coordinating conjunction before the last two words as follows: "… aryloxypropanolamines, trimetoquinols." Examiner has interpreted the claim to read as follows "… arylethanolamines, aryloxypropanolamines and trimetoquinols."

Claim Rejections – 35 USC 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-14 are rejected under 35 USC 112 second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as their invention.

The listing of claims received January 16, 2009 contains typographical errors that result in an apparently unintentional amendment. In each instance in the new listing of claims, the characters "ss; 3" replaced "β_3," "ss; 1" replaced "β_1," "ss; 2" replaced "β_2" and "(3" replaced "β" from the prior claim set. As such, claims 3-14 are not clear or precise with respect to the agonists, antagonists and blockers they describe.

For purposes of examination, examiner has interpreted the claims consistent with the terminology present in the listing of claims received September 26, 2006, as the examiner found no amendments in the new claim set other than the typographical errors.

Claim Rejections – 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-6 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson (Current Problems in Cardiology, cited on applicant's IDS filed May 31, 2007) in view of Wheeldon (Br. J. Clin. Pharmac., cited on applicant's IDS filed May 31, 2007).

As to claim 3, heart failure possesses a variety of risk factors and underlying pathophysiologies, but most generally, heart failure develops when the heart cannot pump as much blood as the body needs. Carson teaches that the clinical syndrome known as heart failure most often begins with an initial insult that impairs systolic function and that, over time, myocardial response to this injury includes remodeling of cellular and heart architecture that further compromises heart function (p. 426 and 427).

Carson does not teach the administration of therapeutically effective amounts of β_3-adrenoreceptor agonists to patients suffering from or susceptible to heart failure or myocardial hypertrophy.

Wheeldon teaches administration of therapeutic amounts of the β_3-adrenoreceptor agonist BRL 35135 to normal male volunteers and that said administration leads to increased systolic blood pressure, increased stroke distance and increased minute distance (p. 364-366).

As to claim 4, an individual that is a member of the patient population with symptomatic heart failure would be expected to have at least one of the clinical symptoms of heart failure, meeting at least one of the optional populations of patients of claim 4.

As to claim 5, Wheeldon teaches administering the β_3-adrenoreceptor agonist BRL 35135, which is an arylethanolamine. Thus, Wheeldon teaches at least one of the optional components of claim 5.

As to claim 6, Wheeldon teaches administering the β_3-adrenoreceptor agonist BRL 35135. Thus, Wheeldon teaches at least one of the optional components of claim 6.

As to claim 9, Wheeldon teaches the additional step of administering a β-adrenoreceptor antagonist, also known in the art as a beta-blocker, e.g. bisoprolol. Thus, Wheeldon teaches the additional step of claim 9.

As to claim 10, Wheeldon teaches the additional step of administering the beta-blocker nadolol. Thus, Wheeldon teaches the administration of the beta-blocker nadolol of claim 10.

As to claim 11, Wheeldon teaches the additional step of administering the beta-blocker bisoprolol, a β_1-adrenoreceptor selective antagonist. Thus, Wheeldon teaches the administration of at least one of the optional components of claim 11.

As to claim 12, Wheeldon teaches the additional step of administering a beta-blocker, e.g. bisoprolol, prior to administration of a β_3-adrenoreceptor agonist, e.g., BRL 35135. Thus, Wheeldon teaches at least one of the optional steps of claim 12.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to be motivated treat heart failure patients who have decreased systolic pressure generation as one their clinical symptoms, as taught by Carson, with the β_3-adrenoreceptor agonist BRL 35135, as taught by Wheeldon, because Wheeldon teaches that the β_3-adrenoreceptor agonist BRL 35135 increases systolic pressure generation and cardiac output *in vivo* in humans. Thus, it would have

been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wheeldon with those of Carson to produce the inventions of claims 3-6 and 9-12.

Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson in view of Wheeldon, as applied to claims 3-6 and 9-12 above, and further in view of Gauthier (Gauthier et al., Trends in Pharmacol. Sci., see examiner's Notice of References Cited).

The combination of Carson and Wheeldon have been discussed *supra*. The combination of these references do not teach the β_3-adrenoreceptor agonist BRL 37344. In addition, the combination of these references do not teach β_3-adrenoreceptor agonists further comprising β_1- and/or β_2-adrenoreceptor antagonist activity.

As to claim 7, Gauthier teaches a number of β_3-adrenoreceptor agonists, including the potent β_3-adrenoreceptor selective agonist BRL 37344 (p. 426). Gauthier teaches that BRL 37344 potently activates β_3-adrenoreceptors and only weakly interacts with β_1- and β_2-adrenoreceptors (p. 426 and 427). Thus, Gauthier teaches the β_3-adrenoreceptor agonist BRL 37344 of claim 7.

As to claim 8, Gauthier teaches two β_3-adrenoreceptor agonists further comprising β_1- and/or β_2-adrenoreceptor antagonist activity, e.g., CGP12177 (p. 126). Thus, Gauthier teaches β_3-adrenoreceptor agonists possessing the additional properties of claim 8.

One with ordinary skill in the art would have been motivated to combine the teachings of Gauthier with those of Carson at the time the invention was made since BRL 37344 potently activates β_3-adrenoreceptors and does so selectively, potentially avoiding the β_2-adrenoreceptor-mediated effects produced by the β_3-adrenoreceptor agonist BRL 35135 taught by Wheeldon. Furthermore, Gauthier's teaching that a subset of β_3-adrenoreceptors agonists possess the $\beta_{1/2}$-adrenoreceptor antagonistic properties of a beta-blocker, one of the standard classes of drugs in heart failure, would have been an especially strong motivation to combine considering the fundamental role beta-blockers already play in the therapy of heart failure (p. 426). Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wheeldon, Carson and Gauthier to produce the inventions of claims 7 and 8.

Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carson in view of Wheeldon, as applied to claims 3-6 and 9-12 above, and further in view of Cecil (Cecil Textbook of Medicine, see examiner's Notice of References Cited).

The combination of Carson and Wheeldon have been discussed *supra*. The combination of the Carson and Wheeldon references does not teach at least partially stabilizing the patient prior to administration of one or more β_3-adrenoreceptor agonists. Furthermore, the combination of these references do not teach that the stabilization of a patient may comprise treatment with ACE inhibitors, aldosterone antagonists and/or beta-blockers.

As to claim 13, Cecil addresses the limitation of claim 13 in light of the various classifications of heart failure and the infinite possibilities that a patient may present with on the continuum between susceptibility to heart failure and Stage IV heart failure. For example, Cecil teaches that a variety of approaches are possible including (1) minimizing disease progression and incidence in susceptible patients, (2) interference with neurohormonal systems responsible for cardiac remodeling and progression of the disease in asymptomatic diagnosed patients and (3) alleviating fluid retention, lessening disability and reducing the risk of further progression when the disease has already manifested (p. 216). Cecil teaches that the above may involve a multi-pronged approach to the disease including diuretics, as well as neurohormonal (sympathetic and renin-angiotensin systems) and hemodynamic interventions (p. 216-217). Most importantly, Cecil teaches that for patients with life threatening heart failure, the initial principal objectives are to stabilize the precarious state of the circulation and maintain end organ function until precipitating factors have resolved or until a strategy for treating the underlying disease can be formulated (p. 217).

As to claim 14, Cecil teaches that the use of ACE inhibitors is indicated in mild, moderate and severe heart failure to aid stabilization of the disease (p. 222). The above represents at least one of the optional possibities of claim 14.

One with ordinary skill in the art would have been motivated to combine the teachings of Cecil with those of Carson stems from Cecil's teaching that stabilizing individuals before formulating and implementing a therapeutic strategy is a fundamental methodology in advanced heart failure management. Thus, it would have been prima

facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wheeldon, Carson and Ceil to produce the inventions of claims 13 and 14.

Claim Disposition

Claims 3-14 are rejected at this time. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to WELDON PHILLIPS JR. whose telephone number is (571)-270-7673. The examiner can normally be reached Monday through Thursday & every other Friday between 7:30 AM and 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/WP/
Examiner, Art Unit 4121

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4121